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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,723	09/17/2001	Michael Kramer	113.1012	3340

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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,723	KRAMER ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *2-7 and 9-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election with traverse of Group IV, claims 1 and 8, in the reply filed on May 12, 2006 is acknowledged. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 2-7 and 9-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1 and 8 have been amended. No claims have been canceled or added. Accordingly, claims 1 and 8 are examined on the merits herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claims recite alleles or derivatives of SEQ ID NO: 8 obtained through amino acid substitution, deletion, insertion or inversion, as well as fragments (partial sequences) of SEQ ID NO: 8 that have the same function as SEQ ID NO: 8. These alleles, derivatives and fragments are functionally identical to a protein that is upwardly adjusted

(overexpressed) in human epidermal keratinocytes that show an elevated expression level of the markers uPA and uPA-R, and they influence cell morphology, cell proliferation, cell adhesion, cell migration and/or cell differentiation. The specification does not explain how a protein can be an allele (a naturally occurring variant of a gene), nor does it explain amino acid inversion or how an amino acid can be inverted to make a derivative. No alleles, derivatives or functional partial sequences (i.e., fragments) of SEQ ID NO: 8 are identified in the specification, either by name or by structure, with the exception of one fragment, SEQ ID NO: 3, which corresponds to the C-terminal portion of SEQ ID NO: 8. Consequently, there is no evidence that any representative species of such large and varied genera, molecules or compounds that are alleles, derivatives or fragments of SEQ ID NO: 8, were in the possession of the inventors at the time of filing, with or without the claimed functional limitations.

To satisfy the written description aspect of 35 U.S.C. 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed. The specification does not disclose any alleles, derivatives or fragments of SEQ ID NO: 8 or 3, apart from SEQ ID NO: 3.

Therefore, the claims fail to satisfy the written description requirement.

Claims 1 and 8 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising SEQ ID NO: 8 or SEQ ID NO: 3 does not reasonably provide enablement for a polypeptide comprising an allele, a derivative or a fragment of SEQ ID NO: 8 that has the same functions as SEQ ID NO: 8, apart from the

fragment of SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether or not undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome

classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

The claims are very broad because they recite any allele, derivative or fragment of SEQ ID NO: 8 that is functionally identical to a protein that is overexpressed in human epidermal keratinocytes that show an elevated expression level of the markers uPA and uPA-R and that is suitable for influencing cell morphology, cell proliferation, cell adhesion, cell migration and/or cell differentiation.

2. The nature of the invention.

The invention is designed to provide a polypeptide for diagnosing or treating autoimmune dermatoses, in particular the diseases pemphigus vulgaris and bullous pemphigoid.

3. The state of prior art.

As discussed below, Nagase et al. ("Prediction of the coding sequences of unidentified human genes. XII. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro," DNA Res 5(6):355-364, 1998). Nagase et al. disclose a protein designated KIAA0903 (GenBank record no. BAA74926), which contains a calponin homology

domain and has 100% sequence identity to amino acids 115-1076 of SEQ ID NO: 8 (see enclosed sequence alignment).

4. The relative skill in the art.

The relative skill in the art as it relates to the claimed invention is characterized by that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

Because it is not known how to identify and select alleles, derivatives and fragments of SEQ ID NO: 8 that have the same functional properties as SEQ ID NO: 8, the specification needs to have more detail as how to make and use the invention. Based on the prior art and the instant specification, one skilled in the art would not be able to identify alleles, derivatives or fragments of SEQ ID NO: 8 that have any functional properties, apart from the fragment of SEQ ID NO: 3. Therefore, one of skill in the art would not be able to predict the effect on the functional properties of SEQ ID NO: 8 of adding, deleting, or substituting any number of amino acids at any positions to make the claimed derivatives or fragments. One of skill in the art would have no idea whether any of these derivatives or fragments would have any utility or function. Because the specification does not provide guidance for the claimed polypeptide with respect to alleles, derivatives and fragments (apart from SEQ ID NO: 3), it cannot be predicted that such polypeptides can be identified.

6. The amount of guidance present.

Applicants have not provided any guidance for alleles, derivatives, or fragments of SEQ ID NO: 8, apart from SEQ ID NO: 3.

7. The existence of working examples.

The specification does not provide any working examples disclosing making or using any alleles, derivatives, or fragments of SEQ ID NO: 8. Also, there are no working examples

disclosing using SEQ ID NO: 8 in the diagnosis or treatment of any skin disease or to influence cell morphology, cell proliferation, cell adhesion, cell migration and/or cell differentiation. The only working example not related to cloning or measuring the amount of SEQ ID NO: 8 is Example 5, which discloses that HaCaT cells treated with an anti-sense oligonucleotide to the pKe#83 gene showed increased differentiation compared to untreated cells.

8. The quantity of experimentation necessary.

To prove that all alleles, derivatives and fragments of SEQ ID NO: 8 may be claimed in the instant invention, that is, that they all have the functions of SEQ ID NO: 8 (they influence cell morphology, cell proliferation, cell adhesion, cell migration and/or cell differentiation and are functionally identical to a protein that is overexpressed in human epidermal keratinocytes that show an elevated expression level of the markers uPA and uPA-R), many experiments would have to be conducted under a wide range of conditions. First, several large groups of polypeptides would have to be prepared and then identified as influencing cell morphology, cell proliferation, cell adhesion, cell migration and/or cell differentiation, as well as identified as functionally identical to a protein that is overexpressed in human epidermal keratinocytes that show an elevated expression level of the markers uPA and uPA-R. One group of molecules would somehow have to be alleles of the polypeptide SEQ ID NO: 8 (although genes cannot be polypeptides), one group of molecules would have to be derivatives (polypeptides that differ by any number of amino acid additions, deletions and substitutions at any number and permutation of amino acid positions relative to SEQ ID NO: 8, each substituted amino acid being any amino acid), and one group of molecules would have to be fragments (any number of amino acids deleted from SEQ ID NO: 8 at any arrangement of positions, all the molecules having the same functional properties). Each molecule in each group would have to be tested under a range of conditions (polypeptide concentration, cell concentration, buffers, temperatures, cell types, cell

source (species of cell donor, e.g., human, mouse, rat, fly, yeast, bacterium, such as *E. coli*, etc.). The data from each group of molecules would have to show that each allele, derivative or fragment is functionally identical to SEQ ID NO: 8.

These types of experiments and data are missing from the specification. A great deal of guidance is needed to establish that the claimed polypeptide may be any allele, derivative or fragment of SEQ ID NO: 8, because these are claimed while no alleles or derivatives and only one fragment are disclosed. Because these claimed alleles, derivatives and fragments of SEQ ID NO: 8 have not been disclosed and cannot be determined without a great deal of experimentation, they cannot be predicted. Even if one allele, derivative or fragment could be identified, and data under one set of conditions in one experiment obtained, without a very large amount of data, such a result could not be expected with a different allele, derivative or fragment (such as a substitution derivative vs. a deletion derivative) in an assay under different conditions, such as a different peptide or cell concentration, even using cells of the same type.

In view of the foregoing, the claims fail to satisfy the enablement requirement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Firstly, the claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. For example, the claim recite that the claimed polypeptide is "upwardly adjusted," rather than expressed at an elevated or increased level relative to that in normal human keratinocytes. The claims recite an "amino acid

sequence indicated in SEQ ID NO: 8 sequence protocol" rather than amino acid sequence comprising SEQ ID NO: 8 and "the nucleotide sequence indicated or in sequence protocol SEQ ID NO: 8" rather than the nucleotide sequence encoding the protein of SEQ ID NO: 8, as SEQ ID NO: 8 is a protein sequence. Although sequence protocol is almost identical to the German word for sequence listing, the claims are still required to be written in correct standard English and in compliance with U.S. patent practice.

Secondly, the term "suitable for" in both claims is unclear and does not appear in the specification. Thus, it is undefined, and the meaning of the claims is unclear. MPEP 2111.04 notes that claim scope is not limited by terms such as suitable for, adapted for, and adapted to, claim language that suggests or makes optional but does not require steps to be performed (influencing cell morphology, proliferation, adhesion, migration or differentiation in the instant case), or claim language that does not limit a claim to a particular structure.

Thirdly, claim 1 is confusing and does not entirely make sense because it recites a polypeptide comprising SEQ ID NO: 8 or an allele or derivative thereof. Alleles are naturally occurring variations of genes. Polypeptides cannot be alleles. Consequently, the claim is interpreted as being drawn to a polypeptide comprising SEQ ID NO: 8 or a derivative thereof. Also, the claim recites that the derivative is obtained through amino acid inversion. Amino acid inversion is not defined or explained in the specification, and this portion of the claim cannot be examined because it has no meaning.

Fourthly, claim 8 is confusing and does not entirely make sense because it recites a polypeptide resulting from a splice variant of an mRNA which comprises the nucleotide sequence indicated or in sequence protocol SEQ ID NO: 8, or the nucleotide sequence complementary to one of these two, or a partial sequence of one of these nucleotide sequences, or a nucleotide sequence that hybridizes wholly or in part with one of these

nucleotide sequences, wherein said peptide ... . It cannot be determined what Applicants meant to claim. A claim cannot be drawn to one polypeptide and multiple polynucleotide sequences, and SEQ ID NO: 8 is a polypeptide sequence. In response to the restriction requirement, Applicants elected to have the polypeptide of SEQ ID NO: 8 examined. Accordingly, claim 8 is interpreted as being drawn to the polypeptide of SEQ ID NO: 8 or a part thereof that has the functional limitations recited in the wherein clause in this claim. To put the claim into clear and definite language, Applicants may amend this claim to read as follows (or cancel claim 8 and add a new claim to read as follows):

An isolated polypeptide (or an isolated polypeptide encoded by a splice variant mRNA) comprising the amino acid sequence of SEQ ID NO: 8 or a partial sequence thereof which is expressed at an elevated level in activated human epidermal keratinocytes having elevated expression of the activation markers uPA and uPA-R, wherein the polypeptide influences cell morphology, cell proliferation, cell adhesion, cell migration and/or cell differentiation.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1 and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by Nagase et al. ("Prediction of the coding sequences of unidentified human genes. XII. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro," DNA Res 5(6):355-364, 1998). Nagase et al. disclose a protein designated KIAA0903 (GenBank record

no. BAA74926), which contains a calponin homology domain and has 100% sequence identity to amino acids 115-1076 of SEQ ID NO: 8 (see enclosed sequence alignment). The protein of Nagase et al. is a derivative of SEQ ID NO: 8, a deletion derivative, and it is a fragment of SEQ ID NO: 8. Applicants disclose that SEQ ID NO: 3 and SEQ ID NO: 8 have the same functions (see paragraphs 12, 15 and 21 of the specification), and both are referred to as pKe#83. Therefore, SEQ ID NO: 3 appears to be or contain the functional portion of the protein. Because the protein of Nagase et al. comprises SEQ ID NO: 3, it also has the same functions as SEQ ID NO: 8. Therefore, a holding of anticipation is required.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rosanne Kosson
Examiner, Art Unit 1653

rk/2006-05-24

Rosanne Kosson

ROBERT A. WAX
PRIMARY EXAMINER